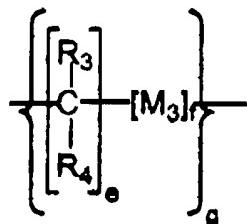


B. TERMINAL DISCLAIMER Re USSN 09/823,296

A terminal disclaimer is enclosed to obviate a provisional double patenting rejection over commonly-assigned USSN 09/823,296. It is urged that the rejection has been rendered moot.

C. REJECTIONS UNDER 35 U.S.C. § 102**Claims 1-15, 17-20 and 23-31 Are Not Anticipated By U.S. Patent No. 5,620,689**

At page 3 of the Office Action, the Examiner has repeated the rejection of the subject matter of the above mentioned claims under 35 U.S.C. §102(b), as being anticipated by U.S. Patent No. 5,620,689 (hereinafter the '689 patent). In response, Applicants have amended the claims to further define the invention and distinguish over the reference. Specifically, as pointed out in the telephone interview, the independent claims have been amended to require the spacer moiety:



to be present. This element is not described in the '689 patent. Therefore the pending claims are not anticipated by the cited reference. In addition, there is no disclosure or suggestion to add the spacer groups claimed herein. As pointed out in the paragraph bridging pages 5 and 6 of the specification, the extenders between the polymer residue ends and the parent therapeutic molecules have several advantages over the prior art. For example, they allow the polymer-based prodrugs to have a more predictable degree of loading. The substantially uniform polymeric conjugates are thus easy to analyze and are highly reproducible. The rate of hydrolysis is also predictable and reproducible from batch to batch. In view of the foregoing, it is respectfully urged that the Examiner reconsider and remove the rejection and pass the application to allowance.

D. FEES

This response is being filed within the shortened statutory period for response and therefore no fee is believed to be due. If, on the other hand, it is determined that any further fees are due or any overpayment has been made, the Assistant Commissioner is hereby authorized to debit or credit such sum to Deposit Account No. 02-2275.

Pursuant to 37 C.F.R. 1.136(a)(3), please treat this and any concurrent or future reply in this application that requires a petition for an extension of time for its timely submission as incorporating a petition for extension of time for the appropriate length of time. The fee associated therewith is to be charged to Deposit Account No. 02-2275.

E. CONCLUSION

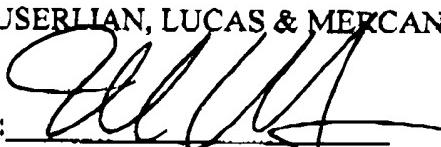
In view of the actions taken and arguments presented, it is respectfully submitted that the present application is now in condition for allowance.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,

MUSERLIAN, LUCAS & MERCANTI, LLP

By:


Michael N. Mercanti
Reg. No. 33,966

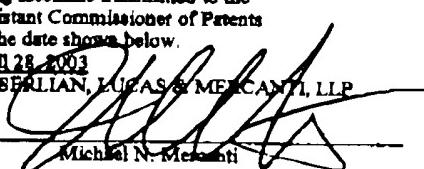
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April 28, 2003

MUSERLIAN, LUCAS & MERCANTI, LLP

BY:


Michael N. Mercanti

Docket No. 213.1116U

UNITED STATES PATENT AND TRADEMARK OFFICEExaminer: **RILEY, JEZIA**

Art Unit: 1637

Re: Application of:

GREENWALD, R. B. et al.

Serial No.:

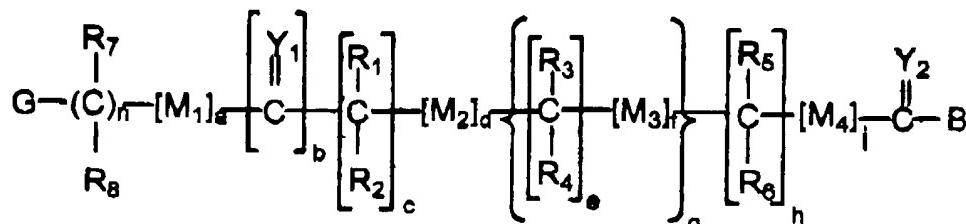
09/823,283

Filed:

March 29, 2001

For: **POLYMER CONJUGATES OF BIOLOGICALLY ACTIVE AGENTS AND EXTENSION MOIETIES FOR FACILITATING CONJUGATION OF BIOLOGICALLY ACTIVE AGENTS TO POLYMERIC TERMINAL GROUPS****APPENDIX J- Version with markings to show changes made****IN THE CLAIMS:****Claim 1 has been amended as follows:**

1. (Amended) A compound comprising the formula:



wherein:

G is a linear or branched polymer residue;**Y₁** and **Y₂** are independently O, S, or NR₉;**M₁-M₃** are independently O, S, or NR₁₀;**M₄** is X or Q;wherein X is an electron withdrawing group and Q is a moiety containing a free electron pair positioned three to six atoms from C(=Y₂);**B** is a residue of an amine-containing moiety or a residue of a hydroxyl-containing moiety;**R₁₋₁₀** are independently selected from the group consisting of hydrogen, C₁₋₄ alkyls, C₂₋₁₂ branched alkyls, C₃₋₈ cycloalkyls, C₁₋₆ substituted alkyls, C₃₋₈ substituted cycloalkyls, aryls,

substituted aryls, aralkyls, C₁₋₆ heteroalkyls and substituted C₁₋₆ heteroalkyls;

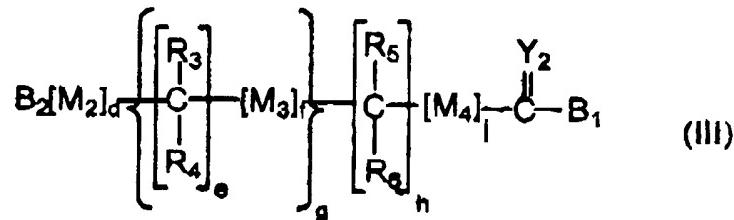
a, b, c, d, [e, f, g], h, i and n are each independently zero or a positive integer; and e, f and g are each independently a positive integer.

Claim 4 has been amended as follows:

4. (Amended) The compound of claim 1, wherein *a, b, c, d, [e, f, g], h, i and n are independently zero, one or two.*

Claim 25 has been amended as follows:

25. A method of preparing a polymeric conjugate, comprising:
 a) reacting a biologically active moiety having an unprotected amine or hydroxyl group with a compound of the formula



wherein

B₁ is a leaving group capable of reacting with an unprotected amine or hydroxyl group;

B₂ is a cleavable protecting group;

Y₂ is O, S, or NR₉;

M₂-M₃ are independently O, S, or NR₁₀;

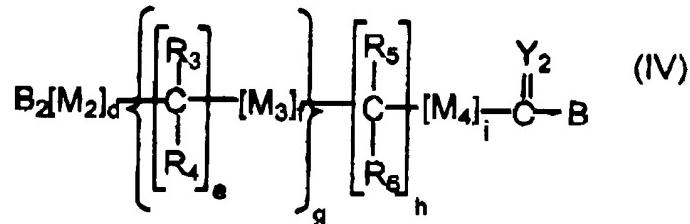
M₄ is X or Q;

wherein X is an electron withdrawing group and Q is a moiety containing a free electron pair positioned three to six atoms from C(=Y₂);

R₃₋₆, R₉ and R₁₀ are independently selected from the group consisting of hydrogen, C₁₋₆ alkyls, C₃₋₁₂ branched alkyls, C₃₋₈ cycloalkyls, C₁₋₆ substituted alkyls, C₃₋₈ substituted cycloalkyls, aryls, substituted aryls, aralkyls, C₁₋₆ heteroalkyls and substituted C₁₋₆ heteroalkyls;

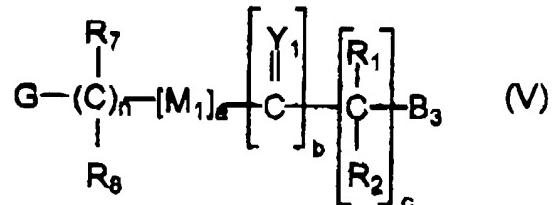
d, [e, f, g], h, and i are each independently zero or a positive integer; and

e. f and g are each independently a positive integer
to form a protected intermediate of the formula:



wherein

- B is a residue of an amine-containing moiety or a residue of a hydroxyl-containing moiety;
 b) deprotecting the resultant intermediate by removing B_2 ; and
 c) reacting the deprotected intermediate with a compound of the formula



wherein

B_3 is a leaving group;

G is a polymer residue;

Y_1 is O, S, or NR_9 ;

M_1 is O, S, or NR_{10} ;

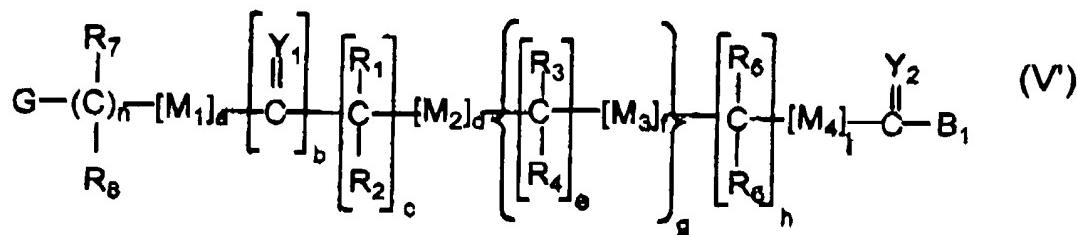
$\text{R}_1, \text{R}_2, \text{R}_7, \text{R}_9$ and R_{10} are independently selected from the group consisting of hydrogen, C_{1-6} alkyls, C_{3-12} branched alkyls, C_{2-8} cycloalkyls, C_{1-6} substituted alkyls, C_{1-8} substituted cycloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} heteroalkyls and substituted C_{1-6} heteroalkyls; and

a, b and c are each independently zero or a positive integer, whereby a polymeric conjugate is formed.

Claim 26 has been amended as follows:

26. A method of preparing a polymeric conjugate, comprising:

reacting a polymer-spacer intermediate of the formula



wherein

B_1 is a leaving group capable of reacting with an unprotected amine or hydroxyl group;

G is a polymer residue;

Y_1 and Y_2 are independently O, S, or NR_9 ;

M_1-M_3 are independently O, S, or NR_{10} ;

M_4 is X or Q;

wherein X is an electron withdrawing group and Q is a moiety containing a free electron pair positioned three to six atoms from $C(=Y_2)$;

B is a residue of an amine-containing moiety or a residue of a hydroxyl-containing moiety;

R_{1-10} are independently selected from the group consisting of hydrogen, C_{1-4} alkyls, C_{1-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls, C_{3-8} substituted cycloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} heteroalkyls and substituted C_{1-6} heteroalkyls;

a, b, c, d, [e, f, g], h, i and n are each independently zero or a positive integer; and

e, f and g are each independently a positive integer;

and thereafter reacting intermediate with a biologically active moiety having an unprotected amine or hydroxyl group to form the polymeric conjugate.

New claim 32 has been added:

--32. (New) The compound of claim 1, wherein e, f and g are each independently one or two. --.

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MUSERLIAN, LUCAS & MERCANTI, LLP

BY: _____

Michael N. Mercanti

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PTO-2038 (02-2000)

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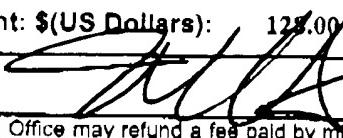
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